Remarks

Reconsideration of the application is respectfully requested in view of the foregoing amendments and following remarks. Claims 1-7, 10-30 and 33-48 were pending in this application. Claims 1, 10, 12, 14, 16, 19, 20, 23, 33, 35, 36, and 39 are amended herein. Claims 6, 7, 11, 15, 17, 29, 30, 34, 38, 40, and 48 are canceled and new claims 49-56 are added. Therefore, claims **1-5, 10, 12-14, 16, 18-28, 33, 35-37, 39, 41, 43-47, and 49-56** are currently pending in this application. Applicants believe no new matter is added herein. Applicants believe that the application will be in condition for allowance following entry of this amendment.

Applicants thank the Examiner for stating that claims 43-47 are allowed. Applicants also thank the Examiner for withdrawing the previous rejection under 35 U.S.C. § 112, first paragraph, written description.

Telephone Interview

Applicants thank Examiners Archie and Navarro for the courtesy of a telephone interview with their representative, Susan W. Graf, on August 14, 2008. During the telephone interview, the rejections under 35 U.S.C. § 112, first paragraph were discussed. Potential claim amendments were discussed to address the § 112 rejections. Applicants believe that this amendment addresses the concerns that were discussed regarding the § 112 rejections.

Rejections under 35 U.S.C. § 112, first paragraph

Enablement

Claims 1-7, 10-30 and 33-41 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Applicants request reconsideration in light of the amendments presented herein.

Claims 1, 19, 20, and 23 are amended herein to recite methods "wherein the suppressive oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO:

13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, or a combination of two or more thereof." Support for this amendment may be found in the specification, for example, at page 21, lines 11-21 and Table 1 (page 22). Further, the specification defines the characteristics of the suppressive oligodeoxynucleotides (ODNs) for use in the claimed methods as having the characteristics of at least about 8 nucleotides in length, forms a G-tetrad, a CD value greater than about 2.9, and at least two guanosines (for example, page 3, lines 7-9). The ODNs of SEQ ID NOs: 1-25 include these characteristics, and would be recognized as such by one of skill in the art.

In addition, claims 10, 12, 33, and 35 are amended and new claims 49, 50, 53, and 54 are added to set forth subsets of the claimed oligonucleotides comprising multiple guanosine rich sequences (claims 10, 33, 49, and 53) or about 2 to about 4 guanosine-rich sequences (claims 12, 35, 50, and 54). Similarly, claims 13, 16, 36, and 39 are amended and new claims 51, 52, 55, and 56 are added to set forth subsets of the claimed oligonucleotides comprising at least one TTAGGG motif (claims 13, 36, 51, and 55) or about 2 to about 4 TTAGGG motifs (claims 16, 39, 52, and 56).

Applicants assert that the specification enables one of skill in the art to make and use the invention of the amended claims without undue experimentation. A Wands analysis is provided.

(A) Breadth of claims: The amended claims are limited to methods of treating inflammatory lung disease using suppressive ODNs comprising the sequences of SEQ ID NOs: 1-25, or combinations thereof. The Office asserts that the claimed methods are only enabled for the use of ODNs of the lengths shown in Table 1 (Office action, page 5, last paragraph). The claims are now directed to ODNs comprising the specific nucleic acid sequences shown in Table 1.

(B) Nature of the invention: The claims are directed to methods of treatment that utilize nucleic acid sequences. The Office asserts that "although inflammatory lung disease can be treated there is no treatment for recurrence or prevention of the full development of the disease"

(Office action, page 6, first paragraph). Applicants re-assert that the claims are directed towards methods of treating inflammatory lung disease. The specification defines treating a disease as "a therapeutic intervention that ameliorates a sign or symptom of a disease or pathological condition after it has begun to develop" (page 18, lines 1-2). Further, inhibiting a disease "refers to inhibiting the full development of a disease" (page 17, lines 24-25).

In addition, while Broide *et al.* (*J. Immunol.* 161:7054-7062, 1998; cited by Office, page 6) note the limitations of corticosteroid therapy (page 7054), this article also teaches that immunostimulatory DNA sequences were "effective in inhibiting eosinophilic airway inflammation when administered either systemically (i.p.) or mucosally..." (Abstract). Thus, one of skill in the art at the time of filing of this application would recognize that nucleic acids (such as an immunostimulatory DNA sequence; not the suppressive ODNs of the present application) could be used to treat lung disease.

(C) State of the prior art: Applicants thank the Office for accepting that synthesis of ODNs, administration of ODNs to a subject of interest, and art-recognized models for testing therapies for treatment of inflammatory lung disease are well known in the art.

(D) Level of ordinary skill in the art: Applicants note that the Office accepts that the level of ordinary skill in the art is of a molecular biologist and/or pulmonologist is high. Applicants assert that given the disclosed ODNs of SEQ ID NOs: 1-25, one of skill in the art could make and use the claimed invention.

(E) Level of predictability in the art: Production of ODNs comprising the sequences set forth as SEQ ID NOs: 1-25 is routine in the art. Further, Applicants note that the Office accepts that there are art recognized models for inflammatory lung disease that can be used to test the effects of the ODNs of interest. These are described in the specification. Exemplary results in a model system are provided in the Examples section.

(F) Amount of direction provided: The specification provides the sequences of the ODNs for use in the claimed methods (for example, Table 1, page 22). The specification further provides pharmaceutical compositions and methods of administration of ODNs (for example, page 24, line 9 to page 30, line 10) and methods for determining the effectiveness of an ODN, such as by monitoring lung function or by measuring cytokine or chemokine production (for example, page 30, line 11 to page 31, line 26).

(G) Working examples: The specification provides the sequences of ODNs for use in the claimed methods and provides the use of an exemplary ODN (SEQ ID NO: 1) in inhibiting an immune response *in vitro* (Example 2) and in an animal model of inflammation (Example 3).

Applicants emphasize that the presence of only one working example is not sufficient reason for an enablement rejection. MPEP § 2164.02. Rather, "one must evaluate all the facts and evidence and state why one would not expect to extrapolate that one example across the entire scope of the claims." MPEP § 2164.02. The specification provides suppressive ODNs of SEQ ID NOs: 1-25 and describes characteristics of ODNs that are useful in the claimed methods: (1) are 10-30 nucleotides in length, (2) have a CD value of greater than about 2.9 (for example, see the specification on page 20, lines 15-24), and (3) form a G-tetrad (for example, see the specification on page 20, lines 7-14). SEQ ID NOs: 1-25 include these characteristics and the specification demonstrates that SEQ ID NO: 1 is effective as demonstrated by Examples 2 and 3. Thus, there is no reason that one of skill in the art would expect that ODNs comprising the sequences of SEQ ID NOs: 2-25 would not be effective in the claimed methods.

Further, additional ODNs from the group of sequences of SEQ ID NOs: 2-25 have subsequently been shown to be useful in suppression of immune activation. For example, Yamada *et al.* (*J. Immunol.* 169:5590-5594, 2002; submitted herewith as **Exhibit A**) shows that suppressive ODNs H154 and 1502 (Table 1, SEQ ID NOs: 1 and 20, respectively) inhibit IFN-γ production by BALB/c spleen cells stimulated with CpG DNA or bacterial DNA (see *e.g.* Figure 1, page 5591). Further, Gursel *et al.* (*J. Immunol.* 171:1393-1400, 2003; submitted herewith as **Exhibit B**) show that ODNs having the sequences of SEQ ID NOs: 1, 2, 3, 4, 7, and 12 suppress CpG DNA induced cytokine production in BALB/c spleen cells (see *e.g.,* Figure 3A (SEQ ID NOs: 2, 3, 4, and 7) and Figure 3D (SEQ ID NOs: 1 and 12), page 1396). In addition, *in vivo* administration of the suppressive ODN of SEQ ID NO: 2 inhibited CpG ODN stimulated cytokine production in mice (Gursel *et al.* Figure 5, page 1398). Finally, Shirota *et al.* (*J. Immunol.* 174:4579-4583, 2005; submitted herewith as **Exhibit C**) teach that suppressive ODN A151 (SEQ ID NO: 2) inhibits IFN-γ production in BLAB/c mice treated with and LPS (see *e.g.*, Figure 5A, page 4581). Both CpG and LPS stimulate the release of pro-inflammaotry cytokines and are models for lung inflammation (see *e.g.* specification page 35, lines 18-20). These examples clearly show that the ODNs disclosed in the specification can be used in the claimed methods.

(H) Experimentation needed: Applicants assert that given that the amended claims are limited to the ODNs comprising SEQ ID NOs: 1-25, it would require only routine experimentation for one of skill in the art to formulate the ODNs for use in the described methods to assess effectiveness of an ODN, such as by monitoring lung function or by measuring cytokine or chemokine production (for example, page 30, line 11 to page 31, line 26).

Based on the foregoing arguments, it would not require undue experimentation for one of skill in the art to make and use the claimed invention. Therefore, Applicants assert that the claims as amended are enabled by the specification and respectfully request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Written Description

Claims 1-7, 10-30, 33-41 and 48 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants request reconsideration in light of the amendments herein.

The Office asserts that the ODNs recited of at least about 12 and at most 30 nucleotides in length, forms a G-tetrad, and at least two guanosines does not provide sufficient guidance as to the structure of the suppressive ODNs that function in the claimed methods. Applicants respectfully disagree with this assertion. However, solely to advance prosecution, claims 1, 19, 20, and 23 are amended herein to recite methods "wherein the suppressive oligodeoxynucleotide comprises the nucleic acid sequence set forth as one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID

NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, or a combination of two or more thereof…"

In addition, claims 10, 12, 33, and 35 are amended and new claims 49, 50, 53, and 54 are added to set forth subsets of the claimed oligonucleotides comprising multiple guanosine rich sequences (claims 10, 33, 49, and 53) or about 2 to about 4 guanosine-rich sequences (claims 12, 35, 50, and 54). Similarly, claims 13, 16, 36, and 39 are amended and new claims 51, 52, 55, and 56 are added to set forth subsets of the claimed oligonucleotides comprising at least one TTAGGG motif (claims 13, 36, 51, and 55) or about 2 to about 4 TTAGGG motifs (claims 16, 39, 52, and 56).

The ODNs comprising SEQ ID NOs: 1-25 are clearly set forth in the specification, for example at page 21, lines 11-21 and their sequences are presented on page 22, Table 1. Applicants were clearly in possession of the claimed subject matter at the time of filing and respectfully request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Conclusion

Applicants believe the present application is ready for allowance, which action is requested. If any matters remain to be discussed before a Notice of Allowance is issued, Examiner Archie is respectfully requested to contact the undersigned for a telephone interview at the telephone number listed below.

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 595-5300
Facsimile: (503) 595-5301

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By /Susan W.Graf/
Susan W. Graf, Ph.D.
Registration No. 60,432

cc: Docketing